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Establishment of Nutritional Requirements in Man

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In speaking of nutritional requirements we are accustomed to use the terms "minimum requirement," "optimum requirement," "allowance for safety," "recommended allowance," etc. These terms have been useful and may be necessary. It should be recognized, however, that many facts are lacking and so these terms are extremely difficult to define with precision. The term "minimum requirement" will be generally recognized as the smallest amount of a nutrient which will support normal performance or prevent detectable signs of nutritional deficiency. The "optimum requirement" is the amount required for optimum health. The distinction between these two terms is largely a function of how accurately one can determine the minimal need. The minimum requirement can never be below a level where detectable disability or abnormality occurs. If one can detect improvements in health by amounts above a presumed minimum need, the estimate was too low. On the other hand, the optimum requirement is not above the amount required for maximal performance. Thus, if one assumes a situation where we knew all we want to know, if we had complete confidence in our methodology and if we had done all of the experiments that should be done, the minimum and optimum levels would be identical. This is true whether one is trying to define the requirements of a population or of an individual.

It is clear that we are not in this fortunate position. The tools for assessing optimal health are recognizably inadequate and the ideal experiment has never been done. Obviously, there are insufficient criteria for establishing optimal levels of intake which, it seems to me, should be the same as the recommended allowances. Today we are forced to introduce an "allowance for safety" over and above the minimal estimates. Working from an average minimum requirement, this allowance for safety must include amounts to cover the variation between individual requirements as well as the estimated difference between the minimum and the optimum requirements.

The actual situation is neither so good as many people believe nor as bad as it appears to others. Facts indicate that one need not be pessimistic about present data upon which minimum requirements are based — actually, the reverse seems more realistic. But we must be realistic about our capabilities and the general situation. Data upon which requirements are based are the fundamentals of the science of nutrition. Scientific attitude, economic, agricultural and manufacturing possibilities, dietary habits, and increasing concern about the effects of overnutrition, all make it clear that one cannot be arbitrary about dietary recommendations. To do so is to disqualify nutritionists as scientists.

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Experience has demonstrated that nutritional standards, even when they are based upon inadequate information that turns out to be wrong, are necessary and useful. Only when data from various sources are compared to standards is it possible to evaluate the standards and, if necessary, revise them. The danger lies in universal acceptance of standards without realization of their limitations. Widespread use and custom may often lead to unjustified assumptions as to the accuracy of facts, making revision of established customs extremely difficult.

Variability is, of course, inherent in biology and there is good reason to believe that nutritional requirements of individuals are different. It is inconceivable that this should not be true. Yet, so far as I am aware, no legitimate estimates of this inherent variability have been made. In all studies where requirements have been estimated, a great deal of variation is seen in the performance of the individuals. This variation is the result of a conglomeration of factors, some of which are biologic while others may be classified as errors. The errors include not only the obvious analytical errors, incomplete collections, etc., but errors in the sense that the same experiment done again upon the same individual would undoubtedly not yield the same results. The biologic variation would include not only the inherent differences among individuals but the effects of the past and present environment, including the nutritional environment. The difficulties of sorting out and quantitating these sources of variation are great but not insurmountable, at least for some. The primary difficulty is the general perversity of human subjects and the time and expense involved in working with them. Yet, better experimental design of many of the studies which have been reported in the literature, including my own, could have contributed to solving this fundamental problem. Only when we have reasonable estimates of the accuracy of the methods used to determine requirements and knowledge of the size and cause of the different sources of error, will we be in position to approach this part of the "allowance for safety" adequately.

Incidently, the inability to separate errors from real differences is a continual harassment in the evaluation of all dietary surveys. When one chooses the lower 10 or 20 per cent of intakes of the population surveyed as probably being deficient, these may represent nothing more than those selected by random error. Yet, subjects with these intakes are of primary interest in most surveys. Contrariwise, the mean intake would appear to be a resonably good estimate even though the methods used are known to be rather crude (1).

Mention has been made of the effect of the past nutritional environment as one factor influencing estimates of requirements. That this is true there is no doubt, but the effect varies greatly depending upon the nutrient under study. It is customary to say that an individual is "adapted" to a certain diet or to certain conditions. This term is often used by nutritionists in a somewhat derogatory sense, with the implication that adaptation is a necessary but somewhat undesirable result of feeding a diet less than ideal. This cannot be true in the larger view since all of us are adapted, to a greater or less extent, to our particular way of life and dietary habits. If diets high in nutrients are fed, the adaptation

is just as certain and involves either decreased absorption or increased destruction or excretion of the nutrients in question in order to protect against excessive storage. No *a priori* judgment can be made as to whether adaptation to an inefficient body economy to protect against excessive storage is better or worse than adaptation to an efficient economy to conserve nutrients. Both situations are well known and both are an obvious accommodation to the nutritional environment. Our concern should not be with adaptation *per se* but rather with situations where adaptation is not entirely possible or is incomplete and thus health is impaired.

In all studies with man as the experimental subject, one is working with an "adapted" individual, making definition of "normality" extremely difficult. It is important, nevertheless, to attempt to distinguish or at least bear in mind, the difference between "normal" meaning optimum or maximal health, and "normal" meaning most common, average, or usual. For example, in the discussion of iron in the Recommended Allowances (2), it is stated that the normal man daily excretes about 1.0 mg. of iron and absorbs about 10 per cent of his usual intake. Thus, it is concluded that "a 10 milligram allowance is adequate for adult males." This is possibly true but it must be pointed out that in actuality this is only a description of the necessary mechanics of excretion and absorption in order to maintain balance in adult males consuming about 10 mg. of iron daily, a common intake. Since "There is considerable evidence that adult males can maintain normal hemoglobin concentrations upon very low intakes of iron" (2), it is not certain that these balance data are relevant to the determination of the actual iron requirement.

Studies of calcium balance present similar problems. In Malm's (3) excellent study, three of the 26 men failed to adapt to intake levels of around 400 mg. of calcium per day. That is, although all of the others did come into balance at the lower level of intake after varying periods of time, these three did not during the time of the study. It is not known why, but there are several possibilities. This failure to change calcium excretion levels might represent inherent differences in the men, it might be related to differences in their previous dietary pattern, or it might have been due to facts entirely unrelated to diet or calcium intake. If it were due to the previous diet, was the previous diet optimum in the men who did adapt or in those who did not? The point to be made is that in studies of this kind where "adaptation" is important, we are accustomed to focus our attention upon the diet being fed. Actually, concern should be with a judgment of both the diet being fed and the previous diet. In the calcium balance studies under discussion, if the effect of the previous diet made it impossible for the men to adapt to lower levels of intake, this may be more important than the conclusion that the level of calcium fed in the experimental diet was not adequate to maintain balance.

Malm (3) presents one extremely interesting case. At the beginning of the study one young man was in calcium balance upon the diet fed. Then he started studying for an examination. Although the same dietary calcium intake was

maintained throughout the experiment, as the time of the examination approached the fecal calcium rose — resulting in a strong negative calcium balance. In fact, the fecal calcium eventually exceeded the calcium intake. The examination was postponed, the fecal calcium decreased, and the man came into balance again — all with no apparent change in dietary intake. The utilization of calcium during the examination preparation period became so poor that it is doubtful whether balance could have been maintained at any level of calcium intake. The calcium intake was obviously not the factor involved. If psychological reactions or stress may have such important effects, the problem of having "normal" subjects under comparable conditions becomes formidable indeed. Complete normality, as defined, is not possible under strict dietary control and particularly when the test diet is relatively severe. Some other instances where psychological reactions may have been a dominant factor and superseded the effects of diets under study have been mentioned. Malm cites personal communications from Young and Stearns indicating emotional stress as an important factor in determining calcium balance. Widdowson (4) reported growth responses in children as the result of a more sympathetic school administration. The vague and troublesome personality changes reported in mild thiamine restriction studies (5) have been thought by some to be due to the experiment as much as the diets.

It is readily apparent to all who are actively engaged in nutrition that the intellectual climate and attitudes toward nutrition are changing. They are becoming more objective and critical. Early concern, as late as 10 or 15 years ago, was devoted almost entirely to the prevention of deficiency disease. The enthusiasm for abundant intakes of all nutrients is now tempered, and sometimes overshadowed, by concern over the possible untoward effect of excessive intakes. There are numerous reasons for this shifting emphasis. Deficiency diseases are now rare in the United States. This allows for research and emphasis upon other conditions, particularly the so-called degenerative diseases which are of increasing importance. Obesity is now a well recognized disability. The fundamental causes, although still unkown (6, 7), are clearly related to excess calorie consumption. Methods of treatment are far from satisfactory. Coronary heart disease (8, 9), the major cause of death in prosperous societies, is related to nutrition but only a beginning has been made upon the causal relationships and methods of treatment. Dietary restriction with various nutrients often has an inhibitory influence upon the initiation and development of several tumors studied experimentally (9, 10). Differences in susceptibility to various cancers, as well as to many other diseases, are known in populations throughout the world (12, 13). Not all of these are to the disadvantage of the populations with restricted diets and may be related to nutrition. Hypervitaminosis A and D are continual problems and, in recent years, hypercalcemias in infants (14), possibly related to high vitamin D intakes in conjunction with high calcium intakes, have become a serious problem in some countries. The implicaton that possibly vitamin D may be doing more harm than the rickets it is given to prevent (15) is sobering, if possibly an overstatement. Low calcium diets are accepted as part

of the treatment for kidney stones and the possibility that high calcium intakes are an etiological factor in susceptible individuals, although unproven, deserves consideration. Finally, increased awareness and political and scientific acceptance of some responsibility for medical conditions throughout the world have had two effects. The serious problems of undernutrition were brought home at a time there was a feeling of some complacency. On the other hand, the nutritional possibilities, in spite of relatively restricted diets, also stand out. No one who has seen the excellent physical specimens among the Bantu, for example, living largely upon mealie meal, can help but wonder about the discrepancies between these diets and modern nutrition teaching.

All this means that the scientific nutrition community is charged with the responsibility of defining nutritional needs with increasing accuracy. These must be defined with full recognition of limits at the top as well as at the bottom. All the discussions of individual variation, differences in need, and allowances for safety, apply at the top limits as surely as at the bottom. Fortunately, for a number of the nutrients, the limits of safety in terms of physical health appear rather large. However, for many populations, the agricultural and economic possibilities also apply definite limits. The effect of an entire nutrition program in some countries may be negated if the objectives are not reasonable in terms of the resources.

It is not possible to discuss here the basis for the estimations of requirements and of recommended allowances for each of the nutrients. It may be noted, however, that, in general, data upon requirements derive from three sources: (a) epidemiologic data on the occurrrence or absence of disease in relation to various levels of nutrient intake; (b) data obtained with human subjects in controlled studies deliberately designed for the determination of requirements of a specific nutrient; and (c) studies upon other species. It is probably generally agreed that the studies upon laboratory animals are the most accurate but that the findings cannot be applied to humans unless the correct factors for such translation are reasonably well defined by actual studies upon human subjects. Nevertheless, when certain parameters seem applicable to several species, one has considerable justification in applying the findings to man. Examples which might be mentioned would be the relation of thiamine need to calories, or more specifically to non-fat calories, and the reasonably constant relationship of the vitamin A need to body weight.

It appears that there are common parameters in protein metabolism, minimal protein needs per basal calorie and biological value, which unify data upon protein requirements of various species (16). The FAO Committee on Protein Requirements (17) has, in part, utilized these concepts in arriving at its recommendations. Additional data upon man, particularly growing children, are needed to determine how useful this approach may be and how realistic the derived requirements are.

A rule of thumb that the niacin need is approximately 10 times the thiamine need was based upon studies with dogs and formed the original basis of the

recommended allowance for niacin (18). The complications introduced into niacin requirements by the role of tryptophan (2, 19) as a niacin precursor preclude such a simple relationship although it may still be useful.

For the other nutrients for which dietary allowances have been established — calories, calcium, iron, riboflavin, ascorbic acid, and vitamin D — interspecies comparisons have as yet been much less useful. Recently, Bro-Rassmusen (20) has concluded that the expression of riboflavin data upon a calorie basis may provide a consistent baseline for the various studies upon both man and animals. This might provide some explanation for the occurrence of riboflavin deficiency in Korean troops (21) consuming levels of riboflavin much above those levels believed necessary to prevent clinical symptoms in man in this country (22). The Recommended Allowances for riboflavin assume no relationship to caloric expenditure or basal metabolism and are based upon body weight (2).

In studies upon man himself, whether in controlled experiments or in epidemiologic studies, the data consist of the occurrence or absence of clinical symptoms, functional tests of some kind, or serum or urinary excretion levels of the nutrient or some metabolite derived from it. These, of course, must be considered relative to the intake of the nutrient in question in order to provide data upon nutritional requirements. Epidemiologic data are always somewhat suspect for this purpose in view of the uncertainty of the nutrient intake of an individual. It has been true in many surveys that assessment of nutritional status by dietary history and clinical, and laboratory methods seems to have only about a random chance of selecting the same individual. This in itself is a very sobering result, generally unappreciated — sometimes even denied, by the very people who should be most aware of it. On the other hand, it is heartening that in well conducted surveys, the dietary, clinical, and laboratory tests generally agree upon the nature of the nutrition problem. That is, if riboflavin is a problem, for example, this will be indicated by clinical signs, dietary riboflavin level and urinary excretion level, although these tests may not select the same individuals.

A notable exception, in this regard, is the general assessment of calcium lack as a common dietary problem based entirely upon dietary histories with no supporting clinical or laboratory evidence (23, 24). In this author's opinion, this indicates the need for a reassessment of the dietary standards (25) although others have argued that it is a deficiency in the clinical and laboratory tools. Note also might be taken of the low caloric intakes in much of the world relative to recommended allowances and the lack of evidence of protein deficiency in adults who do not meet the recommended level of protein intake (26). It may be concluded that although the epidemiologic approach is relatively crude for determining requirements, it may well provide the final test of whether the recommendations are reasonable.

Mention has been made of balance studies as a means of estimating nutritional requirements. Unfortunately, for some time the balance method had been the only experimental approach for the study of the protein and calcium requirements. It must be considered as logically true that adults maintained in health

over long periods of time must be essentially "in balance," or in equilibrium. In this sense, adults must be adapted to the diets which support them over years of time and, on the average, the amount they consume must be the amount required to maintain them in this state (27). Without contributory evidence of some kind, the amount required for balance does not indicate whether this "adapted" state, to large amounts or small amounts, is good, bad, or indifferent in terms of health. This is particularly true with regard to calcium, where long periods of time may be required for adaptation to occur. In a recent study of Norwegian prisoners by Malm (3), the mean requirement for balance was estimated to be 0.44 ± 0.15 per day. No effect of age upon the requirement for balance or upon ability to adapt was found.

Balance studies upon protein must be evaluated somewhat differently since adaptation, in the sense that urinary excretions change with changes in intake, occurs rapidly. Hence, one can, with relative ease, determine minimum amounts required for balance but this always requires feeding diets lower in protein than the usual diet, some loss of protein from the body, and doubt as to the significance of the results in terms of health over long periods.

Balance studies upon children must be interpreted differently since positive balance, consistent with the growth rate, must occur. Unfortunately, many balance studies yield retention values which appear to be too high to be real. This is true not only in studies upon man but in studies upon animals as well. Duncan (28) has recently reviewed the literature upon calcium balance in cattle and concluded that the data must be in error since the calcium retained cannot be accounted for in the body of the animals. Much of the data upon nitrogen and calcium retention in children (29, 30, 31) also appear too high. It is possible to have excessive retentions of a nutrient over considerable periods of time, with shifts in body composition not measurable in terms of growth, but these cannot represent the long term performance. Hence the results might be explained in part upon periods of study that are too short. On the other hand, there is reason to believe that in long term studies the errors are not randomly distributed. If there is a bias in such studies it is most likely that there will be overestimation of the intake (excessive zeal in cleaning up the plate for analysis in order to avoid underestimation) and incomplete collection of excreta. The net result would be a slight accumulation of positive balances which assume considerable dimensions over long periods. Whatever the explanation may be, it seems plausible that balance data must make sense with what is known about growth, or the discrepancy adequately explained, before they can be relied upon as estimates of requirements.

Data upon serum or urine levels provide the primary information for the estimates of requirements of the vitamins. Ideally, one hopes to find some abrupt change in the level of the material measured, occurring at an intake somewhat above those levels at which clinical deficiency signs appear, and which may be interpreted as evidence of change in tissue saturation. The available data upon riboflavin excretion are an example of this (32). It must be emphasized that a

mere increase in the serum or urine level of the vitamin after a supplement is given provides no real evidence of benefit to the individual. Additional parameters relating the amount of the supplement to the change in the level measured, to the clinical conditions, etc., must be developed. The great theoretical disadvantage of most of the biochemical tests, particularly those for thiamine, riboflavin, vitamin A and ascorbic acid, is that they do not represent functional tests but simple measurement of the same material fed.

Tests which measure maximal storage, maximal serum levels, kidney threshold, etc., meet with little favor today as methods of estimating requirements for fairly obvious reasons.

The Interdepartmental Committee on Nutrition for National Defense (ICNND) recently published a "Suggested Guide to Interpretation of Nutrient Intake Data" (33) (Table 1). "These guides are intended to apply to 25 year-old physically active males of 67 inches (170 cm.) in height and 143 pounds (65 kg.) in weight, living in a temperate climate and consuming a varied diet." Similar proposals for females or children have not yet been made. Values for calories are not given in the table since these are primarily dependent upon body size, climate, age, and physical activity. The values proposed by the ICNND for evaluation of calorie intakes correspond closely to those proposed by the FAO Committee on Calorie Requirements (34) and the Recommendations of the Food and Nutrition Board (2).

TABLE 1.

SUGGESTED GUIDE TO INTERPRETATION OF NUTRIENT INTAKE DATA

	Deficient	*Low*	*Acceptable*	*High*
Niacin, mg/day	<5	5—9	10—15	>15
Riboflavin, mg/day	<0.7	0.7—1.1	1.2—1.5	>1.5
Thiamine, mg/1000 Cal.	<0.2	0.20—0.29	0.3—0.5	>0.5
Ascorbic Acid, mg/day	<10	10—29	30—50	>50
Vitamin A, I. U./day	<2000	2000—3499	3500—5000	>5000
Calcium, gm/day	<0.3	0.30—0.39	0.4—0.8	>0.8
Iron, mg/day	<6.0	6—8	9—12	>12
Protein, gm/kg	<0.5	0.5—0.9	1.0—1.5	>1.5
Calories	-----	-----	-----	-----

With regard to the word "high" this report states: "This term is used here in the sense of 'high' for the prevention of recognizable clinical deficiencies or definite biochemical evidence of deficiency. Good or satisfactory would be advocated by many to replace this term. Nutrient consumption and biochemical values in the 'high' range will be found in many countries which enjoy a high level of health and productivity. However, the precise health advantages which

attend these 'high' levels are the subject of much difference of opinion and little conclusive evidence."

It will be noted that the ICNND has concluded that "acceptable" intakes may fall below, for some nutrients considerably below, the Recommended Allowances. Undoubtedly, this will be interpreted by many nutritionists as a weakening of nutritional standards. As has been explained already, it should be apparent that this is not necessarily or even probably so. The job facing the nutrition scientist is to define "adequate nutrition" and it is immaterial from the scientific point of view whether this calls for larger or smaller intakes than are customarily consumed or those which have been previously assumed to be desirable. Furthermore, there is no reason to believe that all the foods people eat have to be justified upon a nutritional basis.

The ICNND report is probably the most objective estimate of current knowledge which has been made by an official group. Difficulties in terminology, semantics, and philosophy are still apparent. The interpretation of the term "high," quoted above, leaves open the possibility that such levels may be advantageous and it must be admitted that this is true. No upper limits were established and many of the divisions into "low," "acceptable," and "high" intakes are arbitrary and were clearly influenced (as have been practically all dietary standards established throughout the world) by the Recommended Allowances of the Food and Nutrition Board.

The approach used by the ICNND has several advantages over a single recommended intake or allowance. It provides a means of evaluating the relative severity of nutritional problems which may be encountered. Thus, emphasis would be placed, correctly, upon the most limiting nutrient. The establishment of ranges of intake under the various categories more accurately reflects our current knowledge and implies less finality than a single figure. It can be assumed that these or any other provisional standards will be wrong in various respects and subject to much improvement. However, the evaluation of different diets by various means against the same provisional standard will, in time, provide the data needed for this revision and better definition of the meaning of an "adequate" or "optimum" diet. This definition must be a major concern of everyone with serious and valid interests in this field.

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